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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/879,279	06/12/2001	Gayle Dace	45163-1005	3524
25297	7590	07/13/2006	EXAMINER	
JENKINS, WILSON, TAYLOR & HUNT, P. A. 3100 TOWER BLVD SUITE 1200 DURHAM, NC 27707			EPPERSON, JON D	
		ART UNIT	PAPER NUMBER	
			1639	

DATE MAILED: 07/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/879,279	DACE ET AL.
	Examiner	Art Unit
	Jon D. Epperson	1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 07 April 2006.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 11 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 11 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>10/11/05</u> .	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
	6) <input type="checkbox"/> Other: _____

DETAILED ACTION

Request for Continued Examination (RCE)

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/7/06 has been entered. Claims 1-24 and 31 were pending. Applicants canceled claims 1-10 and 21-31. No claims were added. Therefore, claim 11 is currently pending. An action on the merit follows. Please note any previous indication of allowability is hereby withdrawn in view of the newly cited prior art.

Those sections of Title 35, US code, not included in the instant action can be found in previous office actions.

Information Disclosure Statement

2. The references listed on applicant's PTO-1449 form have been considered by the Examiner. A copy of the form is attached to this Office Action (e.g., 10/11/05).

Withdrawn Objections/Rejections

3. All previous rejections and/or objections are withdrawn in view of Applicants' cancellation of claims 1-10 and 21-31 and/or arguments.

New Rejections*Claims Rejections - 35 U.S.C. 103*

4. Claims 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jakobsen et al. (US Pub. No. 2003/0077609 A1) (Priority to 60/278,598, filed on **March 25, 2001**) (of record) and Cregan et al. (Cregan, P.B.; Mudge, J.; Fickus, E.W.; Marek, L.F.; Danesh, D.; Denny, R.; Shoemaker, R.C.; Matthews, B.F.; Jarvik, T.; Young, N.D. "Targeted Isolation of Simple Sequence Repeat Markers through the use of Bacterial Artificial Chromosomes" *Theor. Appl. Genet.* **1999**, *98*, 919-928) (of record) and Sambrook et al. (Sambrook J. and Russell, D.W. Molecular Cloning: A laboratory Manual. New York: Cold Spring Harbor Laboratory. **January 15, 2001**, Vol. 2, pages 1.1-1.29, 11.35 and 11.98-11.106) (of record, except for pages 1.1-1.29) and Brown (Brown, T.A. Genomes. New York: John Wiley & Sons, Inc. **1999**, pages 18-23 and 136-137) (of record) and Liu et al. (Liu et al. "Development of simple sequence repeat DNA markers and their integration into a barley linkage map" *Theor. Appl. Genet.* **1996**, *93*, 869-876).

For **claim 11**, Jakobsen et al. (see entire document) disclose methods for using modified "locked nucleic acids" (LNAs) for "the isolation, purification, amplification, detection, identification, quantification, or capture of nucleic acids" including applications in gene mapping and/or genotyping (e.g., see Jakobsen et al., abstract; see also page 4, paragraph 43, see also page 6, paragraph 63), which reads on the elected invention. For example, Jakobsen et al. disclose providing one or more modified oligonucleotide conjugates, wherein each of the modified oligonucleotide conjugates comprises at least one locked nucleic acid and a linking molecule (e.g., see Jakobsen et al., paragraph 14 wherein LNAs are disclosed; see also paragraph 49 wherein Applicants'

elected “biotin” species is disclosed; see especially page 7, Example 2, see also paragraph 76; see also paragraphs 53-63). In addition, Jakobsen et al. disclose incubating a sample of nucleic acids with the modified oligonucleotide conjugates, thereby forming one or more hybridized duplexes (e.g., see Jakobsen et al., page 7, Example 2 wherein the “locked” modified oligonucleotide conjugates were used to “hybridize” to a sample of 5’ biotin-labeled 50-mer or 30-mer oligonucleotide, each encompassing 1 to 5 SNPs [single nucleotide polymorphisms] for SNP genotyping; see also page 6, paragraph 55, “In a further aspect, oligonucleotides of the invention may be used to construct new affinity pairs ... The affinity pairs may be used in ... capture and detection of a diversity of the target molecules”; see also paragraph 63, “Assay using an immobilized array of nucleic acid sequences may be used for determining the sequence of an unknown nucleic acid; single nucleotide polymorphism (SNP) analysis; analysis of gene expression patterns from a particular species, tissue, cell type, etc.; gene identification”). Jakobsen et al. further disclose contacting substantially all of the hybridized duplexes with a linking source, such that the linking molecule of each duplex that contacts the linking source forms a bond with the linking source (e.g., see page 7, Example 2, especially paragraph 76 wherein Applicants’ elected “streptavidin” species is disclosed). Finally, Jakobsen et al. disclose separating substantially all of the hybridized duplexes from the sample of nucleic acids (e.g., see page 7, Example 2, especially washing steps).

The prior art teachings of Jakobsen et al. differ from the claimed invention as follows:

For **claims 11**, Jakobsen et al. fail to recite the use of “simple sequence repeat” (SSR) target molecules. Although, Jakobsen et al. teach the use of target molecules like SNPs as physical markers in gene mapping and/or genotyping experiments (e.g., see page 7, Example 2; see also page 6, paragraph 63), Jakobsen et al. fail to explicitly refer to other types of physical markers like SSR target molecules. In addition, Jakobsen et al. fail to expressly state that they use a target simple sequence repeat portion wherein the simple sequence repeat portion of the hybridized duplex is a portion of an insert in a 3.5 kb clone.

However, the combined references of Cregan et al., Sambrook et al., and Brown teach the following limitations that are deficient in Jakobsen et al.:

For **claims 11**, the combined references of Cregan et al., Sambrook et al., and Brown (see entire documents) teach the use of SSRs as target molecules (e.g., see Cregan et al., abstract; see also Brown, page 136, “Mini- and microsatellites” section). Furthermore, the use of “extraction” techniques including the application of streptavidin-coated magnetic beads is also taught (e.g., see Sambrook et al., page 11.99, figure 11-20). The combined references of Cregan et al., Sambrook et al., Liu et al., and Brown also teach the use of SSR portion comprising 1, 2, 3, or 4 base repeats (e.g., see Brown, page 136, column 2, last paragraph wherein CACACACACACACACA is exemplified i.e., a “2 base repeat”; see also Cregan et al., page 919, column 2, last paragraph wherein CA, ATT and ATGT are disclosed i.e., 2, 3 and 4 base repeats).

In addition, the combined references of Cregan et al., Sambrook et al., Liu et al., and Brown teach the use of a 3.5 kb clone (e.g., see Sambrook et al., page 1.16, bottom

paragraph disclosing that smaller plasmids are more durable; see also page 1.19, paragraph 1 showing that the small plasmids are less expensive and easier to purify; see especially, top of page 1.26, “Plasmids ranging in size from 2.6 kb to 85 kb can be introduced ...” showing that plasmids of a 3.5 kb size were routinely used in the art). In addition, the combined references of Cregan et al., Sambrook et al., Liu et al., and Brown teach that plasmid clones can be used to produce clones of simple sequence repeats (e.g., see Liu et al., page 870, column 1, Materials and Methods).

Alternatively, the Examiner contends that the phrase “wherein the simple sequence repeat portion of the hybridized duplex is a portion of an insert in a 3.5 kb clone should not be afforded any patentable weight because it represents intended use of a product-by-process limitation that does not materially change the structure of the simple sequence repeat. See MPEP § 2113, “[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.’ *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).” Here, the “portion” of the clone could consist only of the “insert” and not the “plasmid” (see specification, page 13, line 11), which would not afford any structural difference for the simple sequent repeat. Thus, the process limitation (i.e., making the simple sequence repeat from a 3.5 kb clone) does not appear to provide any patentable weight to the claimed invention in accordance with MPEP § 2113. One of ordinary skill

would expect the product (i.e., the insert) to be the same no matter how it was synthesized and/or prepared.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to capture “simple sequence repeats” (SSRs) as taught by the combined references of Cregan et al., Sambrook et al., Liu et al., and Brown using “locked nucleic acids” (LNAs) as taught by Jakobsen et al. because Jakobsen et al. teach that LNAs possess enhanced specificity/affinity for target sequences and thus can be used to improve all hybridization reactions and specifically point to the PCR based characterization of physical markers commonly used in gene mapping and/or genotyping experiments (e.g., see Jakobsen et al., page 6, paragraph 63; see especially page 7, Example 2), which would encompass the physical markers exemplified by the combined references of Cregan et al., Sambrook et al., Liu et al., and Brown (i.e., the references represent analogous art because “simple sequence repeats” (SSR) and “single nucleotide polymorphisms” (SNP) markers are both PCR-based, co-dominant and abundant molecular markers from eukaryotic genomes that are being widely used in genetic mapping, phylogenetic studies and marker-assisted selection) (e.g., see Brown, pages 18-22 for background information on the use of SNPs and SSRs). In addition, Cregan et al. state that the bacterial artificial chromosomes (BACs) used to isolate SSR markers “can readily be extended to other types of DNA markers, including single nucleotide polymorphisms [i.e., SNPs]” (e.g., see Cregan et al., page 919, column 2, paragraph 1), which would encompass the SNPs disclosed by Jakobsen et al. A person of skill in the art would have been motivated to use the LNAs to search for SSRs because Cregan et al.

state that LNAs provide “enhanced hybridization and [PCR] priming properties” (e.g., see Cregan et al., page 1, paragraph 10; see also page 1, paragraph 11 wherein beneficial PCR results are also disclosed), which would increase the efficiency of searching for the SSRs (just as they do for SNPs) because the SSRs represent PCR-based markers that require hybridization and PCR priming (e.g., see Cregan et al., page 919, column 2, last paragraph). Furthermore, SSRs represent a “preferred embodiment” of physical markers for gene mapping and/or genotyping (e.g., see Cregan et al., page 919, column 2, last paragraph, “The high level of informativeness and co-dominance of microsatellite markers, their widespread occurrence in eukaryotic genomes, and easy amplification via standard PCR technology, make SSR the current marker of choice [i.e., a preferred embodiment] in many species”; see also Brown, page 21, column 1, “Microsatellites [SSRs] are more popular … [because they] are more conveniently spaced through the genome. Second, the quickest way to type a length polymorphism is by PCR, but PCR typing is much quicker and more accurate with sequences less than 300 bp in length [i.e., SSRs]; see also page 21, column 2, wherein the drawbacks of SNPs are outlined e.g., they have only two alleles; see also pages 136-137, “Mini- and microsatellites” section). Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because Cregan et al. state that their BAC technology will work with both SNPs and SSRs and Sambrook et al. state that their streptavidin-coated magnetic beads are particularly well suited for selecting large genomic DNA clones using BACs (see Cregan et al., page 919, column 2, paragraph 1, “This targeted approach to identifying

new DNA markers [i.e., SSRs] can readily be extended to ... single nucleotide polymorphisms"; see also Sambrook et al., page 11.98-11.100, especially figure 11-20).

Furthermore, it would have been *prima facie* obvious to one of ordinary skill in the art to use a plasmid that is 3.5 kb in length to screen for the simple sequence repeats because Liu et al., for example, explicitly state that plasmids can be used for this purpose (e.g., see Liu et al., page 870, Materials and Methods, "The procedures for constructing a small-insert plasmid library and for screening of the SSR-containing clones were as previously described"). In addition, a person of ordinary skill in the art would have been motivated to use plasmids because they are cheap, stable, easy to use via facile PCR and molecular biology techniques, easy to purify, and can be used to produce, screen and sequence a library (e.g., see Liu et al., page 870, column 1, Materials and Methods; see also Brown, page 21, column 1, paragraph 1; see also Sambrook et al., page 1.16, bottom paragraph disclosing that smaller plasmids are more durable; see also page 1.19, paragraph 1 showing that the small plasmids are less expensive and easier to purify; see especially, top of page 1.26, "Plasmids ranging in size from 2.6 kb to 85 kb can be introduced ..." showing that plasmids of a 3.5 kb size were routinely used in the art). Finally, a person of ordinary skill in the art would have reasonably expected to be successful because molecular cloning techniques using plasmids were routinely practiced in the art even with Applicants' claimed simple sequence repeats (e.g., see Sambrook et al., pages 1.1-1.29; see also Liu et al., Materials and Methods).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.

July 7, 2006

JON EPPERSON, PH.D.
PATENT EXAMINER

